Eur Respir J 2013; 41: 1249–1251
DOI: 10.1183/09031936.00053913

EDITORIAL

Lung function, race and ethnicity: a conundrum

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In this issue BRAUN *et al*. [1] make a plea for an international workshop to review aspects of race and ethnicity in relation to lung function. This is a timely initiative, as many people struggle in epidemiological and genetic studies, and in clinical practice, with the interpretation of test results in an increasingly multi-ethnic society [2]. Our notions of race derive from Blumenbach, who defined ''Four varieties of mankind, one species'' (adding a fifth variety in 1781) [3]. Definitions of ''race'' and ''ethnic'' are confusing and often used interchangeably. This ambiguity is reflected in the frequent use of race/ethnicity, a transitional concept adopted for use while phasing out ''race'' from the USA census [4]. At this stage the USA census recognises two ethnicities: ''Hispanic or Latino'', and ''not Hispanic or Latino'', and five races; Hispanic/Latino individuals have a mixed European, African and native American ancestry [5]. American citizens were allowed to self-identify with more than one race in 2000: 2.4% self-identified as multiracial. In sharp contrast, France passed a law in 1978 barring the government from collecting all racial and ethnic data (the Act prohibits collecting ''any information that shows, directly or indirectly, racial or ethnic origins, political, philosophical or religious opinions, trade union membership, moral principles, or information that relates to health or sexual life'' without either the written consent of the individual or an advance recommendation of the National Commission for Information Technology and Civil Liberties, which must first be approved by the Conseil d'État) [6]. The collection of data on race and ethnicity by governments serves administrative and statistical purposes; the classifications should not be interpreted as being scientific or anthropological in nature. However, this caveat is not heeded, and the classifications are widely used in everyday life, science and medicine, where race/ethnicity is used as a proxy for other phenomena.

Humans (*Homo sapiens*) originated in eastern Africa and migrated to the rest of the world [7]. Analysis of microsatellite loci shows progressive loss of genetic diversity as our species grew and spread; genetic variability outside Africa is generally a subset of that within Africa [8]. In general, a species is biologically defined as a group of similar organisms that can reproduce only with each other. Hence, genetically and biologically, *Homo sapiens* is one species, but with genetic diversity. Only 5–15% of genetic variation occurs between large groups living on different continents, the remaining variation occurring within such groups [8]. A clustering algorithm applied to multilocus genotypes from worldwide human populations produced genetic clusters largely coincident with major geographic regions [8], suggesting that global human genetic diversity is a result of gradual variation and isolation by distance rather than major genetic discontinuities.

A widely held view among anthropologists, biologists and sociologists is that race is a socio-political construct based on the notion that groups can be demarcated on the basis of important and clear differences in phenotype, skin colour, ancestry, socio-economic status (SES) and geographical location, *etc*. HOFFMAN [9], a highly respected statistician who was particularly interested in the ''negro problem'' in the US, gave scientific racism its credibility and respectability. He posited that white people were at the top of the hierarchy and social order; ''minority'' racial groups were both biologically inferior and barriers to progress. One of Hoffman's arguments was that ''pure blacks'' had ''inferior vitality'' because their vital capacity (VC) was found to be 6–12% smaller than in whites; this contributed to the belief that the inferior black race, that had a higher death rate, was doomed to extinction. The word ''vital'' in VC, so named by HUTCHINSON [10], and the smaller VC, led Hoffman to a value judgement. His views were contested by contemporary scientists, who pointed out that SES and inequalities in access to medical care, *etc*. should be taken into account in studies of biological differences between ethnic groups [11]. Nevertheless, Hoffman's views remained very influential; they have contributed to great atrocities and still affect personal interactions and social institutions.

Categorising subjects into racial/ethnic groups is done on the assumption that race/ethnicity is a proxy for genetic relatedness; this misrepresents genetic variation and leads to confounding. In general, in studies comparing differences in disease prevalence between two ethnic groups, if an unmeasured environmental variable (such as SES) co-varies in the same fashion as the proportion in one group, a racial difference might be due to this unmeasured variable. For example, in a study of differences in mortality between African and European Americans, BURNEY and HOOPER [12] concluded that the higher mortality in African Americans could only be explained by their lower forced VC [12], reminiscent of the views of HOFFMAN [9]. Correlation does not prove causality: direct analysis of the relevant gene or causative factor is the only reliable way to evaluate risk in an individual.

Race, ethnicity and ancestral categories falsely suggest genetic homogeneity within and heterogenity between groups; they

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ignore the genetic variability within groups, gene–environment interactions [13] and differences due to socially mediated mechanisms. Therefore, many scientists advocate abolishing such categorisation in research [4], *versus* those who believe there is still a role for the continued use of self-identified race and ethnicity in biomedical and genetic research [14–16].

In past decades there have been numerous reports documenting racial/ethnic differences in lung volumes. These may be due to inherent biological differences and/or to confounding factors. A biological perspective is that evolution has given rise to the origin of mammals of widely different size, including *Homo sapiens*. Each species is equipped with a scalable design of lungs and airways [17] which meets the organism's metabolic demands. As *Homo sapiens* gradually spread out of Africa, widely different local conditions (climate, altitude, hunter–gatherer or pastoral life, *etc.*) led to some adaptations. In the process changes occurred in phenotype, giving rise to groups that differ slightly in body build and dimensions. Standing height (H) is commonly used to describe lung size: volumes scale as $\sim H^{2.25}$ [18]. For the same height, the VC and the forced expiratory volume in 1 s (FEV_1) are about 14% smaller in African Americans than in whites [18]. However, standing height is not an ideal scaling factor for lung size, as it does not account for differences in body build. Sitting height (SH) is probably a better proxy for chest dimensions. The SH/H ratio in adult whites is on average ~0.520, in African Americans ~0.505; this can account for half the difference ($100^* (1 - (0.505/0.520)^{2.25}) = 6.4\%$) between groups, in line with some publications [19–21]. For the same age, height and sex the FEV_1/VC ratio is virtually identical in different ethnic groups [18]; hence differences in lung volumes are proportional, with other factors besides body dimensions contributing to ethnic differences. The effect of secular trends in body dimensions [22–24] on thoracic dimensions may alter findings in the offspring of different ethnic groups and lead to secular trends in pulmonary function. Also, an increase in the proportion of mixed-race persons will gradually blur race/ethnic distinctions.

Many factors have been shown to be associated with the level of pulmonary function, among them SES, poverty, education, altitude and chest dimensions [21, 25–28]. That preconceived ideas about lung function and ethnicity are a poor guideline is demonstrated by the fact that predicted values for Mexican and European Americans do not differ [18, 29]. In addition, categorisation into ethnic groups needs to take into account place of birth: Japanese Americans produce larger flow–volume curves compared with Japanese from Japan [30], and US-born Asian Indians have higher pulmonary function values for age and height compared with immigrant Asian Indians [31], suggesting that environmental factors play a role. In this respect it is noteworthy that in Scotland around 40% of Indians were born in India, and just over a third of Pakistanis were born in Pakistan, these proportions being generally lower among younger people [32].

KUMAR *et al*. [33] concluded that genetic variation affects lung volumes. In self-identified African Americans, in whom there is considerable ancestral admixture with genes from Europeans, they found a significant inverse association between lung function and African ancestry, but SES and environmental factors were not taken into account. Yet, this condensed summary shows that a significant proportion of observed differences between populations does not have a genetic basis.

It is clear that race/ethnicity information is sub-optimally reported, that it suffers from highly variable terminology, and that the method of establishing racial/ethnic categories, the rationale for collecting race/ethnicity data, and information on SES are underreported [1, 34]. Use of multi-ethnic prediction equations [18] obviates the need for stigmatising ''race correction''. As the concept of different races is passé, it is high time for a paradigm shift. For lack of a magic bullet the term race/ethnic will continue to be used. However, pending a more satisfactory solution, in aetiological lung function research the methods and rationale for categorisation, including the options offered for self-identification, and additional information including the association with SES should be provided. Hopefully the workshop proposed by BRAUN *et al*. [1] will provide firm guidance on how to proceed from here.

STATEMENT OF INTEREST

None declared.

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